## Pneumococcal Disease (Adult)

*Streptococcus pneumoniae*, or pneumococcus, was first isolated by Louis Pasteur in 1881. It was confused with other causes of pneumonia until the invention of the Gram stain in 1884. By 1940, more than 80 serotypes had been described. It is now estimated that more than 6,000 death each year in the U.S. alone are caused by these bacteria. Antibiotic resistance has also become a serious problem.

*Streptococcus pneumoniae* are gram positive bacteria. There are 90 known serotypes. As with other encapsulated organisms, the polysaccharide capsule is an important virulence factor, and capsular type-specific antibody is protective. Although all serotypes may cause serious disease, a relatively limited number of serotypes cause the majority of invasive infections. Overall, the 10 most common serotypes are estimated to account for about 60% of invasive disease worldwide. But the ranking and serotype prevalence differs by age group and by geographic area. Among children less than 6 years of age in the U.S., seven serotypes account for 80% of isolates from blood or cerebrospinal fluid. In contrast, these same 7 serotypes account for only about 50% of isolates from older children and adults.

Pneumococcus is a frequent inhabitant of the upper respiratory tract and may be isolated from the nose, throat, or both of about 10% of persons at any given time. Carriage rates among children may be even higher. Nearly all persons carry pneumococci at some time during the course of a year. We do not understand why some of these persons go on to develop invasive disease. Host factors, like underlying illness, are probably important. But persons without any underlying illness may also develop invasive pneumococcal disease.

The most common clinical presentation is pneumococcal pneumonia. Among adults, an estimated 100,000 to 135,000 cases of pneumococcal pneumonia requiring hospitalization occur annually in the U.S. Pneumococcus is responsible for up to one third of community acquired pneumonias and up to half of hospital-acquired pneumonias. Pneumococcal pneumonia is also a common complication of influenza and of measles.

Pneumococcal bacteremia can be a severe disease, with an estimated 50,000 cases or more per year. Bacteremia is the most common invasive disease among children. Pneumococcal meningitis is much less common – there are 3,000 to 6,000 cases each year. But pneumococcal meningitis is often fatal, and survivors may have permanent neurologic damage.

Pneumococcus alone is responsible for up to 1 out of every 5 cases of bacterial meningitis in the U.S. Now that Haemophilus influenza is well controlled,

pneumococcus is the most common cause of bacterial meningitis in infants. For all these syndromes, fatality rates are higher in older adults. For example, the fatality rate from pneumococcal meningitis is up to 40% in persons 65 years of age and older.

Pneumococcus is a human pathogen that occurs throughout the world. The reservoir of pneumococcus is believed to be the nasopharynx of human carriers. As I mentioned earlier, up to 10% of persons are colonized with pneumococci at any given moment. Transmission probably occurs mostly from asymptomatic carriers by respiratory droplets. For this reason, a vaccine that could reduce nasopharyngeal carriage could indirectly protect unvaccinated contacts. The communicability of pneumococci is not known with certainty, but transmission can probably occur as long as the organism is present in respiratory secretions.

Much of our knowledge of the incidence and risk factors for invasive pneumococcal disease comes from special studies and surveillance systems. One such special surveillance system is CDC's Active Bacterial Core Surveillance, known as ABCs. This graph shows the incidence of invasive pneumococcal disease by age group, based on data from the ABCs. The vertical axis shows incidence, expressed as rates per 100,000 population. The horizontal axis shows age groups. The highest rates are in children less than 2 years of age. The incidence falls to its lowest point among children 5-17 years of age. The incidence of pneumococcal disease then rises steadily with increasing age. But the incidence of invasive pneumococcal infection in persons 65 and older is less than half that seen in young children. ABCs data suggest that the conjugate vaccine is already having an impact on invasive pneumococcal disease in young children. By 2002, the rate of invasive pneumococcal disease among children younger than 2 years of age had declined approximately 75% compared with the prevaccine era. Disease rates have also declined in older children. We discussed pneumococcal disease in children in more detail in our second session, which you can view as an archived webcast on the Public Health Training Network website.

Although pneumococcal infections occur in healthy persons, there are medical and other factors that increase the risk for disease significantly. Age is an important risk factor for invasive pneumococcal disease. Children 2 years of age and younger are at highest risk. Persons 65 years and older are at increased risk, although rates in this age group are less than half that in young children. Many underlying medical conditions increase the risk of invasive pneumococcal disease. We will come back to this in a moment. Recipients of cochlear implants are a group recently recognized to be at increased risk for invasive pneumococcal disease. A cochlear implant is an electronic device utilized by persons with profound hearing loss that cannot be corrected by hearing aids. There are estimated to be about 25,000 recipients of these devices in the United States. Since 2002, FDA and CDC have been investigating reports of meningitis among recipients of these implants. More than 50 cases of meningitis have been reported in individuals who have had cochlear implants. Two-thirds of these

infections were in young children. The reason why the implants appear to predispose the recipient to meningitis is not known.

Underlying medical conditions that increase the risk of invasive pneumococcal disease include decreased immune function from disease or drugs, functional or anatomic asplenia, chronic heart, pulmonary, liver, and renal disease, and cerebrospinal fluid, or CSF leak. Children who attend out of home day care, and children of certain racial and ethnic groups have increased rates of invasive pneumococcal disease.

So, with more than 100,000 cases of pneumonia and thousands of deaths each year, pneumococcal disease is one of the most common causes of vaccine-preventable death in America. The highest risk is among children less than two, older adults, and people with certain underlying medical conditions. Obviously, this is a disease worth preventing.

The first pneumococcal vaccine was licensed in 1977. It contained polysaccharide from 14 serotypes of pneumococcus. In 1983 a 23-valent polysaccharide vaccine was licensed, which replaced the earlier vaccine. In 2000, the first pneumococcal conjugate vaccine was licensed. This vaccine is recommended only for children. We discussed pneumococcal conjugate vaccine in Session II of the course, so we will limit our discussion today to the polysaccharide vaccine.

Pneumococcal polysaccharide vaccine contains purified capsular polysaccharide antigen from 23 types of pneumococci. These 23 serotypes account for 88% of bacteremic pneumococcal disease, and cross react with types causing an additional 8% of disease. The efficacy of the polysaccharide vaccine has been estimated at 60% to 70% against invasive disease, but appears to vary to some extent with underlying disease. The duration of immunity is 6 years or more, and the schedule is 1 dose, with selective revaccination.

As with other pure polysaccharide vaccines, this vaccine is not effective among children less than 2 years of age. Efficacy also varies among older children and adults, with less protection for persons with chronic illness. Recommendations for the use of pneumococcal vaccine are similar to those for inactivated influenza vaccine. The vaccine is recommended for anyone 65 years of age and older, and anyone 2 years of age and older with a chronic medical condition. The minimum age for pneumococcal polysaccharide vaccine is 2 years, because the vaccine is not effective in children less than 2 years of age. Children less than 2 years of age should receive pneumococcal conjugate vaccine.

The next few graphics list the recommendations for use of pneumococcal polysaccharide vaccine. These slide panels are also in your text. The vaccine is recommended for adults with normal immune systems who have chronic illness. Examples of targeted chronic illnesses are cardiovascular or pulmonary disease, diabetes, and alcoholism. Also included are persons with cerebrospinal fluid leaks, which connect the nasopharynx and the meninges, and are usually the

result of trauma. People with cochlear implants should also be considered at high risk and should also be vaccinated. Adults 65 years of age and older should be vaccinated even if they do not have an underlying illness. People who are immunocompromised should be considered for vaccination. Immunosuppression includes Hodgkin's disease, lymphoma, and multiple myeloma. Persons with chronic renal failure and nephrotic syndrome are relatively immunocompromised and should be vaccinated. Persons with functional or anatomic asplenia are at very high risk of pneumococcal bacteremia and should be vaccinated. Vaccination is also recommended for persons with HIV infection. Children 2 years of age and older who have certain underlying conditions should be vaccinated. These illnesses include functional or anatomic asplenia, sickle cell disease, nephrotic syndrome, CSF leaks, and immunosuppression, including HIV infection. Children with cochlear implants should also be vaccinated. Children at very high risk of invasive pneumococcal disease who are less than 5 years of age should receive **both** pneumococcal polysaccharide **and** pneumococcal conjugate vaccine. Details of this recommendation are included in the "Pneumococcal Disease of Childhood" segment of this course, and in the pneumococcal conjugate vaccine ACIP statement.

Those of you who use pneumococcal vaccine may have noticed that the recommendations for revaccination are a little confusing. The basic problem is that multiple doses of polysaccharide vaccine do not provide a significant boost in antibody titer. In addition, there is little evidence that more than one dose protects any better than just one dose. **Routine** revaccination of immunocompetent persons is not recommended, regardless of the person's age. Revaccination is recommended for persons at highest risk of serious pneumococcal infection, and for those who are likely to have a rapid decline in pneumococcal antibody levels. I will define these groups a little further in a moment.

Revaccination is a one-time event. Data for the safety and efficacy of more than two doses are not available, so only one revaccination dose should be given. This single revaccination dose should be given 5 years after the first dose. For children, a single revaccination dose should be given 3 years after the first dose if the child is 10 years of age or younger at the time of revaccination.

Persons who should be considered for revaccination are those at highest risk of severe disease. This includes persons with functional or anatomic asplenia, and persons with immunosuppression, from either disease or drugs. Disease immunosuppression occurs with HIV infection, leukemia, lymphoma, and other malignancies. Therapeutic immunosuppression occurs with cancer chemo-therapy, post-transplantation immunosuppressive drugs, and high doses of corticosteroids. Revaccination is also recommended for persons with chronic renal failure, and for persons who have conditions that result in a rapid decline in antibody levels, such as nephrotic syndrome. Persons vaccinated before age 65 years should also be revaccinated. Revaccination of healthy persons 65 years of age and older is not routinely recommended. But persons 65 years of age and older should be revaccinated if they received their first dose five or more years earlier, AND were less than 65 years of age at the time of the first dose. Also, if a

healthy person receives the first dose of pneumococcal polysaccharide vaccine at 65 years of age, then develops a disease that places him at high risk – immunosuppression, for instance – a second dose 5 years or more after the first dose would be appropriate. Persons 65 years of age and older whose vaccination status is unknown should be given one dose of vaccine.

Adverse reactions following pneumococcal vaccine are similar to most other inactivated vaccines. Local reactions are reported in 30% to 50% of recipients. Systemic complaints like fever and myalgias are reported in less than 1% of recipients. Severe adverse reactions are rare. Local reactions are reported about 50% more frequently following a second dose of pneumococcal polysaccharide vaccine than following the first dose. But these local reactions are self-limited, and more severe reactions are not significantly more common after a second dose.

Contraindications to pneumococcal vaccine are the same as with most other inactivated vaccines. A history of a severe allergic reaction to a vaccine component or following a prior dose is a contraindication. Moderate or severe acute illness is a precaution, and vaccination should be delayed until the acute illness improves.

We have provided a lot of adult vaccination information for you in the text. You will find it in Appendix C. Among other things there is an excellent review article on Adult Immunization, immunization screening sheets for teens and adults, and the new adult schedule. If your practice deals with adult patients, I would strongly suggest familiarizing yourself with these materials.